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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

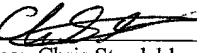
Applicant: MEROT et al. Serial No.: unknown  
Filed: concurrent herewith Docket No.: 8076.147USD1  
Title: METHOD FOR PRODUCING HUMAN HEMOGLOBIN PROTEINS USING  
PLANT CELLS

CERTIFICATE UNDER 37 CFR 1.10

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By:   
Name: Chris Stordahl

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents  
Washington, D. C. 20231

Dear Sir:

In connection with the above-identified application filed herewith, please enter the following preliminary amendment:

IN THE SPECIFICATION

This application is a divisional of application Serial No. 08/983,564, filed June 9, 1998, which is a national stage of PCT/FR96/01123, filed July 17, 1996.

IN THE ABSTRACT

Please enter the abstract attached hereto.

IN THE SEQUENCE LISTING

Please enter the sequence listing submitted herewith.

## IN THE CLAIMS

Please cancel claims 2-42.

Please add and consider claims 43-52 :

43. A hemin protein having the capacity to reversibly bind oxygen, comprising at least one iron-containing porphyrin nucleus, of plant origin, and a protein component comprising at least one polypeptide chain, of animal origin.
44. The protein according to Claim 43, wherein the at least one iron-containing porphyrin nucleus is iron-containing protoporphyrin IX, or a protoporphyrin differing from protoporphyrin IX in the nature of the side chains carried by the  $\beta$  atoms of the pyrrole rings.
45. The protein according to claim 43, wherein the protein component comprises at least one  $\alpha$  and/or  $\beta$ -globin polypeptide chain, or variants thereof comprising one or more amino acid substitution(s), deletion(s) or insertion(s), the hemin protein being capable of binding oxygen reversibly.
46. The protein according to claim 45, wherein the  $\alpha$  or  $\beta$ -globin chain, or variants thereof, comprises in addition a chloroplast targeting signal, a mitochondrial targeting signal, or a N-terminal signal peptide in combination with a signal responsible for retaining a protein in the endoplasmic reticulum or a vacuolar targeting signal.
47. The protein according to claim 45, wherein each  $\alpha$  and/or  $\beta$ -globin polypeptide chain lacks an  $\text{NH}_2$ -terminal methionine.
48. The protein according to claim 43, wherein the protein component comprises at least four polypeptide chains of  $\alpha$  and/or  $\beta$ -globin or variants thereof, each polypeptide chain being bound to an iron-containing protoporphyrin nucleus.
49. The protein according to claim 48, wherein the protein component comprises 2  $\alpha$ -globin chains and 2  $\beta$ -globin chains, or variants thereof.
50. The protein according to Claim 43 wherein said protein binds oxygen with an affinity of between 7 and 40 mm Hg.
51. A pharmaceutical product comprising one or more hemin protein(s) according to Claim 43 in association with a physiologically acceptable excipient.
52. The hemin protein according to claim 51, for the treatment of conditions requiring an improvement in the transport of oxygen in the blood.

REMARKS

Applicants respectfully request that the preliminary amendment described herein be entered into the record prior to calculation of the filing fee and prior to examination and consideration of the above-identified application. Newly presented claims are patterned after claims 15-22 and 38 and 39 of the parent case. Applicants submit the newly presented claims do not raise any issues of new matter.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' primary attorney-of record, Kathryn M. Kowalchyk (Reg. No. 36,848), at 612.371.5311.

Respectfully submitted,

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Dated: October 18, 2001

By Katherine M. Kowalchyk  
Katherine M. Kowalchyk  
Reg. No. 36,848

KMK/kas

## ABSTRACT

A method for producing haemin proteins by (i) inserting into plant cells one or more nucleic acid molecules that each comprise at least one sequence coding for a protein component of an animal haemin protein capable of reversibly binding oxygen, or for a variant or portion of said protein component, and optionally a sequence coding for a selection agent; (ii) selecting cells containing nucleic acid coding for the protein component of the haemin protein; (iii) optionally propagating the transformed cells either in a culture or by regenerating whole transgenic or chimeric plants; and (iv) recovering and optionally purifying a haemin protein that includes a complex consisting of the protein or proteins coded for by said nucleic acid and at least one iron-containing porphyrinic nucleus, or a plurality of such complexes.